However, the Examiner suggests that there is no evidence that such expression levels would have an effect on the host mammal or that such expression levels would correlate to a treatment for a β-glucuronidase deficiency. Further, the Examiner suggests that since the delivery of the neurotrophic virus containing a DNA sequence of interest has not been shown to achieve any therapeutic benefit to the host, the method has not been enabled. Applicants respectfully disagree.

At the outset, it is respectfully pointed out that a demonstration of therapeutic benefit is not a requirement of patentability. The case law is quite clear; Applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Thus, the Examiner's requirement that the specification demonstrate a "therapeutic benefit" is improper.

Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use. *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881, 884 (CCPA 1980) and MPEP §2107.02. If one skilled in the art would accept the data provided as being reasonably predictive of utility in humans, evidence from these tests should be considered sufficient to support the credibility of the asserted utility. *In*

re Hartop, 311 F.2d 249, 135 USPQ 419 (CCPA 1962); *In re Krimmel*, 292 F.2d 948, 953, 130 USPQ 215, 219 (CCPA 1961); *Ex parte Krepelka*, 231 USPQ 746 (Bd. Pat. App. & Inter. 1986) in the instant specification

Accordingly, in an earnest effort to advance the prosecution, Applicants are providing a Declaration by Dr. Laura Plunkett herewith which clearly states that data provided in the instant specification are demonstrative to one of skill in the art of a pharmacological effect and thus, therapeutic utility. See specifically, paragraphs 3 and 4 of Dr. Plunkett's Declaration. Thus, contrary to the Examiner's suggestion, data provided in the instant specification provide one of skill in the art with assurance that the invention delivers genes to the CNS in accordance with the claims. Further, the teachings of the specification can be used in conjunction with general knowledge in the art in establishing strategies for use of this delivery system in humans. See paragraph 4 of Dr. Plunkett's Declaration. Accordingly, the instant specification enables one of skill in the art to make and use the invention to deliver genes to the central nervous systems as claimed.

Further, the Examiner has provided no reasonable basis to question the enablement provided for the claimed invention. See MPEP §2164.04. As stated by the Court:

> it is incumbent upon the Patent Office, whenever a rejection is made on this basis, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

No such evidence has been provided by the Examiner in the instant rejection. In contrast, Applicants are providing Dr. Plunkett's Declaration herewith, which clearly discusses how data provided in the specification are demonstrative of therapeutic utility, thus establishing that there is no reason to doubt the objective truth of statements made in the specification which must be relied on for enabling support. The Examiner also suggests that other neurotropic viruses and routes of delivery have not been shown to have a therapeutic effect in a host. As already discussed in the preceding paragraphs, however, any requirement for a demonstration of therapeutic effect is legally improper. Working examples of every embodiment of the claimed invention are clearly not required. See MPEP §2164.02. The determination of the propriety of such a rejection involves a two stage inquiry. The first stage is to determine how broad the claim is with respect to the disclosure. The second inquiry is to determine if one skilled in the art is enabled to make and use the entire scope of the claimed invention without undue experimentation. The specification clearly teaches other neurotropic viruses at page 10, and routes of administration at page 20, which can be used in the present invention. As

discussed in paragraph 3 of Dr. Plunkett's Declaration, experimental data provided in Example 4 and 5 of the specification wherein the vector was administered through corneal abrasion indicate to one of skill in the art that other peripheral routes of administration would be effective. Thus, the teachings of the specification are commensurate with the scope of the claims.

Accordingly, the instant specification meets the requirements of 35 U.S.C. §112, first paragraph. It is therefore respectfully requested that the objection to the specification and rejection of claims 1-9 be withdrawn.

II. Rejection of Claims 1, 2, 5 and 6 under 35 U.S.C. §102(b)

The rejection of claims 1, 2, 5 and 6 under 35 U.S.C. §102(b) as being anticipated by Dobson et al. has been maintained. Despite arguments presented by Applicants in the previous response filed July 29, 1996, the Examiner continues to suggest that Dobson et al. teaches the delivery of rabbit β-globin gene to the **CNS** of mice. Further, the Examiner suggests that argument presented by Applicants with regard to the fact that Dobson et al. only teach delivery to the PNS are unpersuasive because the statement in the claims "capable of infecting the central nervous system" does not preclude the herpesvirus from infecting another cell as a result of the method. Applicants respectfully traverse this rejection.

At the outset, for clarification of the record, Applicants are providing a Declaration by Dr. Plunkett herewith which makes clear that Dobson et al. **teach only peripheral nervous system delivery**. See specifically paragraph 5 of Dr. Plunkett's Declaration. Accordingly, this reference does **not** teach a method of delivering a selected DNA sequence to the central nervous system of a mammal as claimed.

Further, Applicants respectfully disagree with the reasoning provided by the Examiner in finding arguments in the previous response filed July 29, 1996 unpersuasive.

The case law and the MPEP are quite clear. To anticipate a claim, the reference must teach every element of the claim. See MPEP §2131 and *Verdegall Bros. v. Union Oil Co. of California*. Thus, the relevant question to ascertain whether Dobson et al. is an anticipating reference is whether this reference teaches every element of the instant claim, **not** whether the herpesvirus may infect other cells besides those of the central nervous system.

As is made clear in paragraph 5 of Dr. Plunkett's Declaration, Dobson et al. do **not** teach delivery of a gene to the central nervous system. Accordingly, this reference can not anticipate claims drawn to a method of delivering a selected DNA sequence **to the central nervous system**. Further, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 1 to remove the phrase "capable of" to make clear that the

neurotropic viral vector infects the central nervous system. Thus, Dobson et al. do not anticipate claims 1, 2, 5 and 6 of the instant application and it is respectfully requested that this rejection be withdrawn.

III. Rejection of Claims 3, 4, 7, 8 and 9 under 35 U.S.C. §103

The rejection of claims 3, 4, 7 and 8 under 35 U.S.C. §103 as being unpatentable over Dobson et al. in view of Nishimura has also been maintained. The Examiner suggests that Dobson et al. teach delivery of the rabbit β-globin gene to the CNS. However, this suggestion is incorrect. See Section II, *supra*, and paragraph 5 of Dr. Plunkett's Declaration. Further, the Examiner suggests that Nishimura teaches the DNA sequence for β-glucuronidase and that it would have been within the scope of skills of the ordinary artisan at the time of the instant invention to insert his DNA sequence into recombinant HSV-1 vectors as described by Dobson et al. The Examiner suggests that motivation is offered by Dobson et al. in stating that HSV-1 in a vector for the transfer of genes to neurons.

However, as was pointed out in Section II, *supra*, and in paragraph 5 of Dr. Plunkett's Declaration, Dobson et al. teach that HSV-1 is a vector for transfer of genes to peripheral nervous system neurons which are located **outside** of the central nervous system. In contrast, the claims of the instant invention are drawn

to a method of delivering genes to the central nervous system. In an earnest effort to advance the prosecution, Applicants are amending claim 1 to remove the phrase "capable of" thus clarifying that the neurotropic viral vector infects the central nervous system. As discussed in detail in paragraph 5 of Dr. Plunkett's Declaration, the central nervous system is different from the spinal ganglia in that it is protected from exposure to foreign compounds such as viruses by the blood-brain barrier. Accordingly, the mere fact that Dobson et al. were able to demonstrate delivery of a gene to the peripheral nervous system does not suggest to one of skill in the art that a similar vector could be used to deliver a gene to the central nervous system. Accordingly, the teachings of Dobson et al. alone, or in combination with Nishimura, fail to provide one of skill in the art with a reasonable expectation of success that an HSV-1 vector would deliver a gene to the central nervous system. Thus, this combination of references can not render the instant invention obvious. It is therefore respectfully requested that the rejection of claims 3, 4, 7, 8 and 9 under 35 U.S.C. §103 be withdrawn.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Jane Massey Licata
Registration No. 32,257

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Law Offices of
JANE MASSEY LICATA
Woodland Falls Corporate Park
210 Lake Drive East, Suite 201
Cherry Hill, New Jersey 08002

(609) 779-2400